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Pattern of Ocular Manifestation of HIV/ AIDS among Patients on HAART in ART Clinic of Gondar University Hospital, Northwest Ethiopia

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Abstract

Background: The ocular manifestations of HIV may lead to visual impairment or blindness. In Ethiopia, patients typically initiate antiretroviral treatment (ART) with low CD4 cell counts when the risk of ocular complications may be high.

Objective: To determine the prevalence and types of HIV associated ocular conditions in patients referred for on HAART in Ethiopia.

Methods: This cross-sectional study was undertaken between March 2010 and August 2010 at the ART clinic of Gondar University Hospital, Northwest Ethiopia. Ophthalmic examinations were performed on all consecutive patients satisfying the criteria for enrolment into the ART clinic irrespective of the presence or absence of ophthalmic/visual symptoms.

Results: Enrolled patients (n = 126), of these 70 (57.6%) were females with male to female ratio of 1:1.25 and had a median CD4 cell count of 183 cell/μL (inter-quartile range [IQR], 105-253 cells/μL). About 76.2% of the patients had either Stage I or II. Ninety one (72.3%) of the patients had a CD4 count more than 200 cells/μL at the time of examination. The prevalence of HIV-associated ocular disease was 21.4%. Retinal Microvasculopathy was the commonest finding seen in 9 (7%). The other ocular manifestations noted included: uveitis 4 (3.2%), ophthalmic Herpes Zoster 3 (2.4%), Seborrheic blepharitis 3 (2.4%) and Molluscum contagiosum 3 (2.4%). One patient was found to have disseminated Kaposi sarcoma that had involved the eyelids.

Conclusion: The study demonstrates that HIV/AIDS affects the eyes patients on HAART. It is, hence, recommended that eye care should be a part of the package of medical care in the management of patients on HAART.

Keywords: HIV/AIDS; HAART; Ocular manifestation

Introduction

The HIV/AIDS pandemic continues to present a major health challenge for sub-Saharan Africa, In Ethiopia, adult HIV prevalence in 2009 was estimated to be between 1.4% and 2.8%.[1,2]. The Government of Ethiopia launched fee-based antiretroviral treatment in 2003 and free HAART in 2005. As of July 2010, about 97,000 adults and 4,800 children are accessing HAART services in the country. As HAART becomes more available in this region, we expect the prevalence of HIV-related ocular complications to reduce as seen in the developed world.

HIV-related eye disease may affect 50-75% of HIV infected people worldwide at some point during the course of their illness [3]. This generally takes the form of opportunistic infections that can affect any of the ocular tissues, from the eyelids to the retina. In particular, those conditions affecting the retina may lead to chronic visual impairment or blindness. The spectrum of HIV-related disease appears to differ by geographic location, with reports suggesting that infection-related retinitis is not as common in sub-Saharan Africa compared to industrialized countries and South Asia [4-6].

Before highly active antiretroviral therapy (HAART) was widely available in North America and Europe, 50%–75% of the HIV-infected individuals were estimated to develop non refractive visual problems at some point during the course of their illness and Cytomegalovirus (CMV) retinitis was the leading cause of vision loss [7,8]. The incidence of both ocular complications like Cytomegalovirus retinitis (CMVR) and of visual loss has dropped dramatically in these regions since HAART was made available [9].

The Immune Reconstitution Inflammatory Syndrome (IRIS) is a well recognised complication of Antiretroviral Therapy (ART), which may lead to the clinical deterioration of opportunistic infections due to the rapid restoration of immunological host responses during the initial weeks of treatment [10]. Immune recovery uveitis (IRU) is the predominant form of ocular IRIS and mainly occurs in patients with pre-existing CMVR at the time of ART initiation [11]. IRU is characterised by ocular inflammation following ART initiation and can result in visual loss from macular oedema, retinal neovascularisation and cataract [12,13]. With increasing availability of antiretroviral therapy, IRU may play a significant role in contributing to ocular morbidity. Identification and treatment of ocular disease prior to ART initiation is, therefore, important.

The estimated prevalence of HIV-related eye disease in Ethiopia is reported to be between 60% before free HAART was launched [14]. Given that two-thirds of HIV-infected individuals reside in sub-Saharan

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Africa, the literature on the prevalence or incidence of visual loss due to HIV-related eye diseases in patients on HAART is quite limited. To our knowledge, there have been no studies to date in Ethiopia that have evaluated the prevalence of HIV-related ocular lesions in an unselected, ART population. In this study, we report ocular manifestations of HIV/ AIDS patients on HAART in Northwest Ethiopia.

Patients and Methods

A cross sectional study was conducted among patients who are on HAART at the ART clinic of Gondar University Hospital from November 2010 to February 2011 to determine the pattern and prevalence of ocular manifestations of HIV . Gondar University Hospital is located in Gondar town which is found 740Kms northwest from the capital, Addis Ababa. It is a tertiary referral hospital that serves 5 million populations. The ART clinic has a total of 9,019 patients on follow up out of which 6,022 are currently on HAART.

All patients attending the clinic over a 2-month period were recruited irrespective of ophthalmic symptoms or history or CD4 count. A structured questionnaire was used to assess the socio demographic characteristics that include age, sex, literacy status, occupation and income of the patients. Medical informations were obtained by a combination of direct interview of the patient and review of medical case notes. Data obtained included baseline CD4, present CD4 count, WHO clinical stage, duration since HIV diagnosis, treatment for opportunistic infection and duration of HAART. None of this information was disclosed to personnel conducting the ophthalmic examination. Ophthalmic examinations were conducted by ophthalmologists (FA & YA). Ophthalmic diagnosis was made clinically based up-on slit lamp bio microscopic examination and dilated indirect ophthalmoscope. Relevant laboratory investigations and histopathologic studies were done when the clinical situations dictate. Visual impairment and blindness was defined as per recently revised WHO guidelines, where visual impairment is defined as presenting visual acuity of less than 6/ 18 (0.3 Log MAR), but equal to or better than 3/60 (0.05), and blindness as presenting visual acuity of 3/60 or worse, in the better eye [15]. All patients who were clinically diagnosed were treated accordingly by ophthalmologists. Information was recorded on a pre-coded data collection form and the data were analyzed by SPSS version 15 and p-value less than 0.05 were considered as significant.

Ethical issues

This study was conducted according to the principles expressed in the Declaration of Helsinki. Ethical approval for this study was obtained from the Institutional Review Board of the University of Gondar. Informed consent was obtained from all subjects.

Results

One hundred and twenty-six consecutive HIV-infected participants on HAART (252 eyes) were examined (Table 1). The median age of the 126 patients was 40 years (range: 10-70 years), and 83 (65.9%) patients were female. Majority of HIV patients with ocular manifestations 22(81.5) are unskilled workers. The main sources of referral to the ART clinic were health centers where patients had undergone HIV testing upon relevant history/ examination findings - patients were thus referred to the ART clinic of Gondar University Hospital to receive free ART and HIV management. The median CD4 cell count of participants was 183 cells/μL (Interquartile Range [IQR], 105-253 cells/μL; range, 10 - 521 cells/μL). About Ninety-six (76.2%) participants had symptomatic disease classified as WHO clinical stages

Characteristic	Participants with HIV-related ocular Conditions (%) (n=27)	Participants without HIV related Ocular conditions (%) (n=99)
Age in Years		
<20	0	2(2.0)
20-30	7(25.9)	16(16.2)
31 -40	6(22.2)	36(36.4)
41 -50	9(33.3)	34(34.3)
> 51	5(18.6)	11(11.1)
Gender		
Male	10 (37.0)	33 (33.3)
Female	17 (63.0)	66 (66.7)
Occupation		
Skilled	2(7.4)	11(11.1)
Unskilled	22(81.5)	81(81.8)
None	3(11.1)	7(7.1)
Marital status		
Single	5 (18.5)	19 (19.2)
Married	9 (33.3)	26 (26.3)
Divorced	10 (37.0)	28 (28.3)
Widowed	3 (11.1)	26 (26.3)

Table 1: Socio demographic Characteristics of patients who are on HAART in Gondar University Hospital, Northwest Ethiopia, 2010 (n=126).

Clinical Parameter	Participants with HIV-related ocular Conditions (%) (n=27)	Participants without HIV-related ocular Conditions (%) (n=99)
CD4 count (cells/μ L)		
0-50	0	2(2.0)
51-200	6(22.2)	17(17.2)
201-500	13(48.1)	56(56.6)
>500	7(25.9)	15(15.2)
Not determined	1(3.7)	9(9.1)
WHO clinical stage*		
I	15(55.6)	65(65.7)
II	8(29.6)	8(8.1)
III	4(14.8)	18(18.2)
IV	0	8(8.1)
Months since HIV diagnosis		
<12	2(7.4)	6(6.1)
13-24	7(25.9)	33(33.3)
25-60	16(59.3)	49(49.5)
>61	2(7.4)	11(11.1)
Months since ART started		
<12	1(3.7)	12(12.1)
13-24	7(25.9)	30(30.3)
25-60	18(66.7)	51(51.5)
>61	1(3.7)	6(6.1)
Tuberculosis status		
No history	13(48.1)	54(54.5)
Past history	12(44.4)	41(41.4)
Current on treatment	2(7.4)	4(4.0)
History of eye symptoms		
None	4(14.8)	16(16.2)
Reduced vision	11(40.7)	53(53.5)
Pain	11(40.7)	28(28.3)
Floaters	1(3.7)	2(2.0)

*P<0.01

Table 2: Clinical Profile of patients who are on HAART in Gondar University Hospital, Northwest Ethiopia 2010 (n=126).

I and II and nearly half (46.8%) had either current or a previous history of tuberculosis (pulmonary and extra-pulmonary).

In this study we found a total of 27 (21.4%) patients who had ocular manifestation of HIV/AIDS. Retinal Microvasculopathy was the commonest finding seen in 9 (7%) patients that was seen as cotton wool spot in different retinal quadrants with or without retinal hemorrhages. Other systemic conditions like systemic hypertension and diabetes mellitus were ruled out in such condition. There were 4 cases with uveitis out of which toxoplasmosis retinochoroiditis was diagnosed in 3 (2.4%) patients and one case was idiopathic anterior uveitis. Ophthalmic Herpes zoster was seen in 3 (2.4%) patients with different degree of severity. Seborrheic blepharitis in 3 (2.4%) patients and Molluscum contagiosum of the eyelids in 3 (2.4%) patients were the other clinical conditions observed. There was a case of disseminated Kaposi sarcoma that had involved the eyelids. We have also observed one case of conjunctival lymphoma. There was also one case with anti TB related optic atrophy (Table 3).

Table 4 describes the main eye complications of HIV and their relationship to CD4 count. From the total participants with ocular manifestations, nearly half (48.1%) have a CD4 count of 201-500 cells/μL. Ocular complications were common among patients with higher CD4 count. From the 27 patients with ocular manifestations, retinal microvasculopathy was observed in 4 (14.8%), 3 (11.1%) and 2(7.4%) patients with CD4 counts of 201-500 cells/μL, 51-200 cells/μL and >500 cells/μL, respectively. Majority of opportunistic infections was also found in 6 (22.2%) and 4 (14.8%) patients with CD4 counts of 201-500 cells/μL and 51-200 cells/μL, respectively.

Discussion

This study evaluated the prevalence of ocular disease in HIV-infected patients on ART service in Ethiopia, regardless of whether patients reported ocular or visual symptoms. Ophthalmic manifestations of HIV were found in over a 21.4% of patients which lower prevalence than that reported (60%) before free HAART was launched in Ethiopia [14]. The incidence of CMVR at this institution has decreased significantly with the recent use of HAART therapy. This effect may be related to the aggressive use of HAART and associated immune recovery in this population of AIDS patients. Despite the reduced incidence of CMVR associated with immune recovery, new cases still continue to develop [28]. Moreover, new disease entities such as immune recovery uveitis (IRU) have emerged following the introduction of HAART.

The most common manifestations were Retinal Microvaculopathy, Uveitis, Ophthalmic Herpes zoster, Molluscum Contagiosum and Seborrheic blepharitis. This is almost similar to the frequency of ocular complications reported from a study done in Senegal [11], but was higher than previous reports from Brundi and Malawi (Table 3).

From the overall prevalence of HIV-associated ocular disease in this population, (74.1%) had CD4 counts >200 cells/μL. This result showed that even though many support that ocular manifestations are more important in those with ocular complaints or CD4 counts lower than 200 [7,16,17], they are also seen in patients with high CD4 or those without any ocular complaints. These findings are important with regard to policies for screening of ocular disease prior to ART. Screening in this patient population is particularly important not only because of the high prevalence of disease in this highly immunocompromised patient group but also in view of the potential for worsening of ocular diseases due to ART-induced IRIS.

The fact that more than 74.1% of the patients had CD4 counts >200 cells/μL may partially explain for the higher occurrence of eye manifestations regardless of CD4 count in this study. In this study the most common ocular manifestation observed was Retinal Microvaculopathy (7.1%) which was also most common ocular manifestation in our previous cross-sectional study (24%) before initiation of HAART [14]. The lower prevalence of microvasculopathy (7.1%) as compared to our previous study noted in this study could be due to the fact that most of the patients were on HAART for a longer duration and the consequent decrease in the viral load may lead to a decline in the vasculopathy. Previous cross-sectional studies from other African countries show RM to be the most common, ranging between 10% and 42% [18]. A report from India found microvasculopathy in 50% of the study subjects [6]. The most common types of retinal microvasculopathy were cotton wool spots in different retinal quadrants with or without retinal hemorrhages but their magnitude may be underestimated because they are typically transient and asymptomatic as is the case with this study and others from other African countries.

The most likely causes of uveitis were determined clinically. Four of the patients had uveitis out of which toxoplasmosis retinochoroiditis was diagnosed in 3 (2.4%) patients and one case was idiopathic anterior uveitis. In this study membranes in the pupillary area were the most predominant feature in the anterior segment. This could be due to frequent recurrent uveitis episodes which have been reported as immune recovery ocular inflammation in HAART patients. The possibility of syphilis was considered less likely because serological tests were found to be negative in all the patients with uveitis. Tuberculosis was the most common systemic opportunistic disease in the study subjects though no evidence of ocular tuberculosis was noted in any of the patients with tuberculosis. Ruling out uveitis due to tuberculosis with a greater degree of certainty is difficult. Reports from other studies showed diagnostic challenges and underreporting regarding ocular involvement by tuberculosis and syphilis [19,29].

Ocular diagnosis	Number of Patients (%)
Retinal Microvaculopathy	9 (7.1)
Uveitis	4 (3.2)
Ophthalmic Herpes zoster	3 (2.4)
Molluscum Contagiosum	3 (2.4)
Seborrheic blepharitis	3 (2.4)
Kaposi Sarcoma of eyelid	1 (0.8)
Bacterial keratitis	1 (0.8)
Dry eye	1 (0.8)
Conjunctival lymphoma	1 (0.8)
Neuro-ophthalmic disorders (optic atrophy)	1 (0.8)
Total	**27**

Table 3: Ocular manifestations related to HIV/AIDS in patients who are on HAART in Gondar University Hospital, Northwest Ethiopia, 2010.

CD4 Count (cells/μL)	Complications				
	RM	OI	Tumors	DE	NOD
0-50	-	-	-	-	-
51-200	3	4	2	-	-
201-500	4	6	-	1	1
>500	2	3	-	-	-
Not determined	-	1	-	-	-

RM: Retinal Microvasculopathy; OI: Opportunistic infections; DE: Dry Eye; NOD: Neuro-ophthalmological disorder

Table 4: Ocular manifestations related to HIV/AIDS in patients who are on HAART verses CD_4 count in Gondar University Hospital, Northwest Ethiopia, 2010.

Herpes zoster ophthalmicus accounted for 2.4% of the ocular findings in all HIV/AIDS patients which is lower than has previously been reported in HIV before introduction of HAART [14,20] highlighting the importance of effective HAART in reducing Herpes zoster. In this study, it was found that Herpes zoster ophthalmicus to be an important cause of unilateral complications due to severe involvement of the eyes, late presentation of patients and failure of early referral of patients to ophthalmologists by primary health care professionals.

Molluscum contagiosum was decreased by half from a previous report of 4.8% before free HAART was introduced in Ethiopia [14]. Molluscum contagiosum lesions healing may occur at the initial phase of treatment or later depending on the patient's previous immunological state [21]; however, inflammatory Molluscum contagiosum could be a sign of IRIS after HAART; therefore, attention must be paid to the possible complications associated with the restoration of immunocompetence.

Although Human Herpes Virus-8 (HHV-8) infection is highly prevalent in Ethiopian [22], the study participants almost never develop Kaposi sarcoma, except one case with disseminated Kaposi sarcoma that had involved the eyelids. This is in marked contrast to the strong correlation observed worldwide between HHV-8 seroprevalence and the incidence of Kaposi sarcoma [23]. Elucidation of the mechanism of this postulated resistance to HHV-8 tumorigenicity among Ethiopians should be a target of future study.

In this study, there was no single case with CMVR. This in paradox to the very high rate of CMVR (7.8%) reported in India [24]. The very low prevalence of CMVR seen may not be a direct reflection of lower incidence, but possibly reflect that these patients die from systemic opportunistic infections before their CD4 counts fall low enough to allow the development of HIV-related eye disease [3-5]. The spectrum of HIV-related disease appears to differ by geographic location, with reports suggesting that infection-related retinitis is not as common in sub-Saharan Africa compared to industrialized countries and South Asia [4-6]. This remarkable difference might be explained by the high and early mortality in African patients and, moreover, many patients in Africa spend the last days of their lives at home when they are critically ill [3,25]. It is also possible that HIV subtype, racial variation and co-morbid illnesses could contribute to the rarity of CMV retinitis in developing countries [26]. Being a cross sectional study, this study has taken into account the few number of HIV/AIDS patients and may not be representing the majority that spend the last days of their lives at home and in darkness. In one of the patients dry eye (keratoconjunctivitis sicca) syndrome was detected which may be related to HIV-mediated inflammation and damage of the accessory and major lacrimal glands [27]. Despite the shortcomings, the importance of thorough eye evaluation in resource limited areas has been shown to be helpful in the diagnosis of systemic illnesses with diagnostic challenges.

Conclusion

Current practice at several ART clinics in Ethiopia is to refer patients for an ophthalmic examination only upon complaint of ocular symptoms or after a physician has noted abnormal ocular signs on medical examination. Our findings highlight the need for routine baseline ophthalmic screening at the pre-ART stage. Conducting a full ophthalmic examination requires trained personnel and adequate resources that may be difficult or impossible to provide for all patients in resource-limited countries. However, where possible, we suggest all patients diagnosed to have HIV infection should undergo ophthalmic examination prior to commencing ART and during ART in order to reduce HIV-related ocular morbidity in the era of increased ART availability in Ethiopia. Even though the ocular manifestations are more important in those with ocular complaints or CD4 counts lower than 200, according to results of this study, they are also seen in patients with high CD4 or those without any ocular complaints.

With the advent of increased ART availability, life expectancy for HIV-infected persons is likely to improve. However, the burden of HIV-related ocular disease is likely to remain stable or even increase with possible immune reconstitution ocular complications. Strategies for screening high-risk populations for HIV-related ocular disease are needed as well as provision for the management and treatment of these conditions once detected. Finally, further work is indicated to formally evaluate the validity of patients' symptoms in detecting different types of HIV associated ocular disease.

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